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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

IN RE APPLICATION OF

ROBL ET AL.

APPLICATION NO: DIVISION OF APPLICATION SERIAL NO. 10/008,154 FILED DECEMBER 4, 2001

FILED: HEREWITH

FOR: HMG-COA REDUCTASE INHIBITORS AND METHOD

Art Unit: 1625

Examiner: Evelyn Mei Huang

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

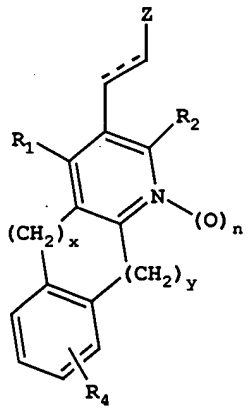
PRE-EXAMINATION AMENDMENT

Sir:

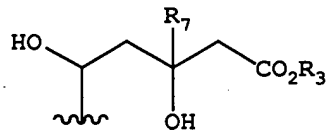
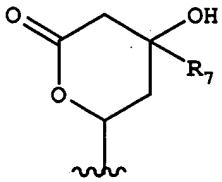
Please amend the claims of the subject application to read as follows.

Please cancel Claims 1 to 11, 13, 16, 37 to 40 and 45.

17. (Amended) A pharmaceutical combination comprising the HMG CoA reductase inhibitor compound having the structure



wherein

Z is  or  also referred to as the δ-lactone;

n is 0 or 1;

x is 0, 1, 2, 3 or 4;

y is 0, 1, 2, 3 or 4, provided that at least one of x and y is other than o; and optionally one or more carbons of $(CH_2)_x$ and/or one or more carbons of $(CH_2)_y$ together with additional carbons form a 3 to 7 membered spirocyclic ring;

R_1 and R_2 are the same or different and are independently selected from alkyl, arylalkyl, cycloalkyl, alkenyl, cycloalkenyl, aryl, heteroaryl or cycloheteroalkyl;

R_3 is H or lower alkyl;

R_4 is halogen, CF_3, hydroxy, alkyl, alkoxy, carboxyl, carboxyalkyl-, aminoalkyl, amino, alkanoylamino, aroylamino, cyano, alkoxyCON(R_{10})-, $R_{11}R_{12}NCO_2$-, $R_{11}R_{12}NCO$-, $R_{13}SO_2N(R_{10})$-, $R_{11}R_{12}NSO_2N(R_{10})$-, $R_{13}OCO_2$- or $R_{13}OCO$;

R_{13} is alkyl, arylalkyl, cycloalkyl, alkenyl, cycloalkenyl, aryl, heteroaryl or cycloheteroalkyl;

R_{11} and R_{12}, and R_{10} are the same or different and are independently selected from H, alkyl, arylalkyl, cycloalkyl, alkenyl, cycloalkenyl, aryl, heteroaryl or cycloheteroalkyl;

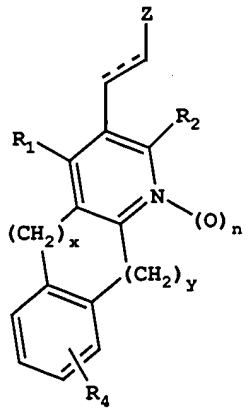
or R_{11} and R_{12} may be taken together with the nitrogen to which they are attached to form a stable 3 to 8 membered ring, which, where applicable, includes 1 to 3 heteroatoms in the ring.

R_7 is H or lower alkyl;

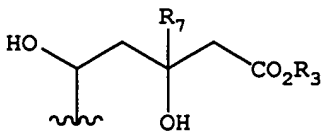
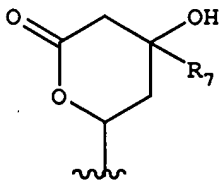
and  represents a single bond or a double bond (which may be cis or trans);

or a pharmaceutically acceptable salt thereof (when R_3 is H), or an ester thereof and or a stereoisomer thereof, and another therapeutic agent which is one or more hypolipidemic agents or lipid-lowering agents, or lipid agents, or lipid modulating agents, and/or one or more other types of therapeutic agents including antidiabetic agents, anti-obesity agents, antihypertensive agents, platelet aggregation inhibitors, anti-dementia agents, anti-Alzheimer's agents, anti-osteoporosis agents, and/or hormone replacement therapeutic agents, and/or other cardiovascular agents (including anti-anginal agents, anti-arrhythmic agents, anti-atherosclerosis agents, anti-inflammatory agents, anti-arthritis agents, anti-platelet agents, anti-heart failure agents), anti-cancer agents, anti-infective agents, hormone replacement agents, growth hormone secretagogues, selective androgen receptor modulators, and/or immunomodulatory agents.

42. (Amended) A method for treating cholesterol related diseases, diabetes and related diseases, cardiovascular diseases, cerebrovascular diseases, which comprises administering to a mammalian species in need of treatment a therapeutically effective amount of a combination of a compound having the structure



wherein

Z is  or  also referred to as the δ-lactone;

n is 0 or 1;

x is 0, 1, 2, 3 or 4;

y is 0, 1, 2, 3 or 4, provided that at least one of x and y is other than o; and optionally one or more carbons of $(CH_2)_x$ and/or one or more carbons of $(CH_2)_y$ together with additional carbons form a 3 to 7 membered spirocyclic ring;

R_1 and R_2 are the same or different and are independently selected from alkyl, arylalkyl, cycloalkyl, alkenyl, cycloalkenyl, aryl, heteroaryl or cycloheteroalkyl;

R_3 is H or lower alkyl;

R_4 is halogen, CF_3, hydroxy, alkyl, alkoxy, carboxyl, carboxyalkyl-, aminoalkyl, amino, alkanoylamino, aroylamino, cyano, alkoxyCON(R_{10})-, $R_{11}R_{12}NCO_2$-, $R_{11}R_{12}NCO$-, $R_{13}SO_2N(R_{10})$-, $R_{11}R_{12}NSO_2N(R_{10})$-, $R_{13}OCO_2$- or $R_{13}OCO$;

R_{13} is alkyl, arylalkyl, cycloalkyl, alkenyl, cycloalkenyl, aryl, heteroaryl or cycloheteroalkyl;

R_{11} and R_{12}, and R_{10} are the same or different and are independently selected from H, alkyl, arylalkyl, cycloalkyl, alkenyl, cycloalkenyl, aryl, heteroaryl or cycloheteroalkyl;

R_7 is H or lower alkyl;

and ⁄⁄ represents a single bond or a double bond (which may be cis or trans);